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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SAOUD, CHRISTINE J	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 08/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/705,476	ACHEN ET AL.	
	Examiner	Art Unit	
	Christine J. Saoud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *77-111* is/are pending in the application.

4a) Of the above claim(s) *77-96,104 and 105* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *97-103 and 106-111* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/915,795.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/13/05, 11/12/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group II, claims 97-103 and 106-111 in the reply filed on 11 May 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 77-96 and 104-105 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11 May 2006.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

The information disclosure statements filed 12 November 2003 and 13 July 2005 fail to comply with 37 CFR 1.98(a)(1), which requires the following: (1) a list of all patents, publications, applications, or other information submitted for consideration by the Office; (2) U.S. patents and U.S. patent application publications listed in a section

separately from citations of other documents; (3) the application number of the application in which the information disclosure statement is being submitted on each page of the list; (4) a column that provides a blank space next to each document to be considered, for the examiner's initials; and (5) a heading that clearly indicates that the list is an information disclosure statement.

Applicant has provided copies of information disclosure statements which were filed in the parent applications, including copies of PTO-892 forms sent to Applicant from the Examiner in those cases. These copies of the PTO-892 forms do not appear to be a proper submission according to 37 CFR 1.98(a)(1). Applicant did not review the IDS forms for duplicate information and did not include the correct application number on each page of the list. It is requested that in future submissions, care is taken to comply with 37 CFR 1.98(a)(1), as well as refraining from listing duplicate citations. The IDS filed 13 July 2005 failed to list the author's names with the citations (see MPEP 609). Lastly, there are two documents which were submitted on 13 July 2005 which are not accounted for on any of the IDS's filed. One document appears to be an examination report – any references associated with this report should be submitted to the PTO in the form of an IDS with copies of the references. The other document is in Japanese, and therefore, the Examiner cannot determine the patent number or filing date because the Examiner does not read Japanese and it does not appear on the IDS filed 13 July 2005.

Sequence Compliance

Applicant's statement regarding the content of the paper copy of the Sequence Listing and the CRF is defective because it does not include the statement that the paper copy and the CRF contain no new matter. A new statement regarding the Sequence Listing is required.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Objections

Claims 97-103 and 106-111 are objected to because they depend from non-elected claims. Appropriate correction is required.

Claim 101 is objected to because there is a typographical error ("labeled" is misspelled as "labeld"). It is also suggested that the word "the" be inserted before the word "label".

Claim 102 is objected to because the word "is" is missing in the phrase "wherein the label an enzyme label".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

> art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 110-111 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The instant specification fails to teach the inventive concept of antibodies which inhibit binding of VEGF-D to a particular receptor subtype (i.e. VEGFR-2 or VEGFR-3). The specification discloses antibodies at pages 11-13 of the specification, including antagonistic antibodies. However, the disclosure that the antagonist (i.e. antibody) may prevent the action of VEGF-D by "preventing the binding of VEGF-D to its corresponding receptor or target cell" (page 13, paragraph [0040], is not a description of antibodies which specifically inhibit binding to a particular receptor subtype. Therefore, the claims are directed to subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Furthermore, there is no evidence that such antibodies were made in the instant specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 97-103 and 106-111 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

All of the claims are directed to antibodies which bind an "isolated mature bioactive VEGF-D polypeptide", however, this recitation fails to convey any structure to the polypeptide encompassed by the claims, therefore, the antibodies which bind it are unclear. Antibodies are proteins which bind epitopes on proteins and the amino acid sequence structure dictates which antibodies would be encompassed by the claims. Without a clear definition of what is encompassed by "mature bioactive VEGF-D polypeptide", the claims directed to antibodies which specifically bind this protein are indefinite. The specification discloses at page 40, paragraph [00108], that VEGF-D is processed to give a mature and fully active protein. However, the structure of that protein does not appear to be defined. The specification discloses that VEGF-D is cleaved to give a C-terminal fragment and in internal peptide, but again, the structure of these proteins are also not described and it is not clear which of these proteins would be the mature bioactive VEGF-D polypeptide.

Additionally, the recitation of VEGF-D does not convey any particular structure for the polypeptide in the claims. This is because vascular endothelial growth factors belong to a family of growth factors which has many members and not all researchers who discover new VEGF molecules name the proteins the same way. Therefore, Applicant's VEGF-D may be someone else's VEGF-3 or VEGF-gamma, etc. Without a clear recitation of structure (i.e. amino acid sequence), the metes and bounds of VEGF-

D cannot be determined, and the skilled artisan would not be able to determine if they had possession of an antibody which specifically binds.

Claims 97 and 106-109 recite the limitation that the antibody "specifically binds a mature VEGF-D polypeptide". The use of "a" conveys the interpretation that there is more than one mature form of VEGF-D. As pointed out above, the mere recitation of VEGF-D is indefinite because the metes and bounds of what are encompassed by this term are not clear. This is further complicated by the fact that there could be many different proteins that are encompassed by "mature VEGF-D".

Claim 102 is directed to a labeled antibody wherein the label is an "enzyme label, or a biotin/avidin system". However, it is not clear how a label can be a "system". The label could be biotin or avidin or streptavidin, but it is not a "system", therefore the metes and bounds of the claim are unclear.

Claims 107-109 are indefinite because they depend from claims 83-85, which include the limitation "consisting essentially of an amino acid sequence", which is indefinite. A polypeptide can comprise a sequence of amino acids and it can consist of a sequence of amino acids. However, without any indication or disclosure of what portion of the sequence is the essential portion, claims to "consisting essentially of an amino acid sequence" is indefinite because it is not clear what portion is essential. Would it be that portion that provides for a biological activity? Or since the claims are directed to antibodies, would it be that portion what provides for antigenic activity? Would an amino acid sequence which is 51% identical to SEQ ID NO:5 be considered "consisting essentially of" or would it need to be greater than that? It would seem that

"essentially" is a term of degree and the metes and bounds of such cannot be determined.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 97-103 and 106-111 are rejected on the ground of nonstatutory double patenting over claims 1-22 of U. S. Patent No. 6,383,484. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent and the application are claiming common subject matter, as follows: antibodies which specifically bind to a VEGF-D polypeptide. The polypeptide of the patent is a VEGF-D which has an N-terminal and C-terminal truncation, however, the limitations of a mature bioactive VEGF-D and consisting essentially of amino acids 101-196, 93-201

and 92-205 of SEQ ID NO:5 appear to be met by the 109 amino acids of SEQ ID NO:1 of the patent because the polypeptide of the patent is completely contained within the polypeptide of SEQ ID NO:5 of the instant application. Therefore, the antibodies of the '484 patent would clearly bind to the polypeptides of the instant application, and therefore anticipate the claims of the instant application. The claims of the instant application are not specifically directed to the monoclonal antibodies of the '484 patent, therefore, the rejection is not a statutory double patenting rejection. The claims, if allowed, would improperly, would improperly extend the "right to exclude" already granted in the patent.

Claims 97-103 and 106-111 are directed to an invention not patentably distinct from claims 1-22 of commonly assigned U.S. Pat. No. 6,383,484. Specifically, the claimed antibodies are a genus of antibodies which bind VEGF-D, whereas the antibodies claimed in '484 are individual species of antibodies. The claims of '484 meet the limitations of the claims of the instant application and if presented in the instant application, would not have been restricted as a separate invention.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). It is not clear if the patent '484 and the instant application are commonly assigned. If commonly assigned, U.S. Pat. 6,383,484, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the

conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

Claims 97-103 and 106-111 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 29-32 and 53-54 of copending Application No. 10/161,694. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both directed to antibodies and compositions thereof that specifically bind to the same protein, VEGF-D.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 97-98 and 106-109 are rejected under 35 U.S.C. 102(e) as being anticipated by Hirata et al. (U.S. Pat. No. 6,828,426).

Hirata et al. disclose a polypeptide (SEQ ID NO:1) which is 100% identical to the polypeptide of the instant application (SEQ ID NO:5), which is called VEGF-D. Hirata et al. disclose antibodies which specifically bind the polypeptide of SEQ ID NO:1 (column 2, line 35), including polyclonal and monoclonal antibodies (column 4, lines 10-15). Therefore, Hirata et al. anticipates the instant claims.

Claims 97-98, 100, 103 and 106-109 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hirata et al. (U.S. Pat. No. 6,828,426).

The disclosure of Hirata et al. is as described above. Hirata et al. further discloses that the antibodies can be used as therapeutic agents (column 6, lines 3-4 and column 11, lines 3-5). While Hirata et al. does not specifically state that the antibodies would be in a pharmaceutical composition, their use as therapeutic agents would specifically and necessarily require a pharmaceutical composition, including a pharmaceutically acceptable carrier or adjuvant. Therefore, Hirata et al. either anticipates or makes obvious the claims directed to pharmaceutical compositions because this formulation would be required for the disclosed use of the antibodies as therapeutic agents.

Hirata et al. also discloses the use of antibodies against VEGF-D for diagnosing diseases (column 6, lines 6-7 and column 12, lines 3-5). While Hirata et al. does not specifically state that the antibodies could be labeled, their use as diagnostic agents would almost necessarily require that the antibodies be labeled so that they could be detected easily. Therefore, Hirata et al. either anticipates or makes obvious the claims directed to an antibody labeled with a detectable label because use of the antibody as a diagnostic would necessarily require detection of the antibody.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 97-98, 100-102 and 106-109 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hirata et al. in view of Alitalo et al. (U.S. Pat. No. 6,221,839).

The disclosure of Hirata et al. is as described above. Hirata et al. do not specifically disclose an antibody labeled with a detectable label.

Alitalo et al. teach antibodies to a VEGF molecule, and indicate that the antibodies can be used in diagnostic applications and that these antibodies can be labeled to be used as imaging agents (see column 3, line 61 to column 4, line 11), including labels which meet the limitations of claims 101-102.

It would have been *prima facie* obvious to add a detectable label to the antibody of Hirata et al. for the purpose of using the antibodies diagnostically as suggested by Hirata et al., because Alitalo et al. teach that such labels are useful for diagnostic applications, including imaging. One would be motivated to label the antibodies, as Alitalo et al. did because the use of a detectable label is very useful in these applications as taught by Alitalo et al. One would further be motivated to label the antibodies of Hirata et al. because Hirata et al. suggest using the antibodies for similar purposes as Alitalo et al. and Alitalo et al. teach that such labeling is useful. One would have a reasonable expectation of success because the antibodies of Alitalo et al. bind a VEGF molecule and the antibodies of Hirata et al. also bind a VEGF molecule, so one would expect very similar results. Therefore, the invention as a whole would have been *prima facie* obvious at the time it was made, absent evidence to the contrary.

Claims 97 and 103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hirata et al. in view of Alitalo et al.

The disclosure of Hirata et al. is as described above. Hirata et al. do not specifically disclose antibodies in pharmaceutical carriers. Alitalo et al. teach antibodies to a VEGF molecule, and indicate that the antibodies can be used to block or activate the Flt4 receptor (column 4, lines 2-3) as well as for controlling endothelial cell proliferation and lymphangiomas (column 4, lines 32-33). Alitalo et al. do not specifically state that the antibodies could be placed into a pharmaceutically acceptable carrier, but Alitalo et al. do disclose pharmaceutical compositions for the polypeptides, which are useful therapeutically. Because the antibodies are taught to be useful for therapeutic applications, similarly to the polypeptides, and the polypeptides are placed into pharmaceutical compositions, it would be prima facie obvious to one of ordinary skill in the art to also place the antibodies into pharmaceutical compositions because such compositions are desirable when a compound is being used in a therapeutic manner to patients. It, likewise, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to incorporate the antibodies of Hirata et al. into pharmaceutical compositions because Hirata et al. teach that the antibodies can be used as therapeutic agents (column 6, lines 3-4 and column 11, lines 3-5) and Alitalo et al. teach that compounds useful as therapeutic agents should be placed into pharmaceutical compositions. Therefore, the invention as a whole would have been prima facie obvious at the time it was made, absent evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine J. Saoud whose telephone number is 571-272-0891. The examiner can normally be reached on Monday-Friday, 6AM-2PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CHRISTINE J. SAOUD
PRIMARY EXAMINER
Christine J. Saoud